Amendments to the Claims:

This listing will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (original) A method for selecting siRNA comprising selecting an siRNA molecule of 19 – 25 nucleoside bases, said method comprising:
   (a) selecting a target gene;
   (b) measuring the functionality of sequences of 19 – 25 nucleotides in length that are substantially complementary to a stretch of nucleotides of the target sequence, wherein said functionality is dependent upon non-target specific criteria.

2. (original) The method according to claim 1 wherein said functionality is determined by applying one of the following formulas:

Formula I = $-(GC/3) + (AU_{15\text{-}19}) - (Tm_{20°C})*3 - (G_{13})*3 - (C_{19}) + (A_{19})*2 + (A_3) + (U_{10}) + (A_{14}) - (U_5) - (A_{11})$;

Formula II = $-(GC/3) - (AU_{15\text{-}19})*3 - (G_{13})*3 - (C_{19}) + (A_{19})*2 + (A_3)$;

Formula III = $-(GC/3) + (AU_{15\text{-}19}) - (Tm_{20°C})*3$;

Formula IV = $-(GC/2) + (AU_{15\text{-}19})/2 - (Tm_{20°C})*2 - (G_{13})*3 - (C_{19}) + (A_{19})*2 + (A_3) + (U_{10}) + (A_{14}) - (U_5) - (A_{11})$;

Formula V = $-(G_{13})*3 - (C_{19}) + (A_{19})*2 + (A_3) + (U_{10}) + (A_{14}) - (U_5) - (A_{11})$;

Formula VI = $-(G_{13})*3 - (C_{19}) + (A_{19})*2 + (A_3)$;

Formula VII = $-(GC/2) + (AU_{15\text{-}19})/2 - (Tm_{20^\circ C})*1 - (G_{13})*3 - (C_{19}) + (A_{19})*3 + (A_3)*3 + (U_{10})/2 + (A_{14})/2 - (U_5)/2 - (A_{11})/2$;

wherein in Formulas I – VII:

$AU_{15\text{-}19}$ = 0 – 5 depending on the number of A or U bases on the sense strand at positions 15 -19;

G_{13} = 1 if G is the base at position 13 on the sense strand, otherwise its value is 0;

C_{19} = 1 if C is the base at position 19 of the sense strand, otherwise its value is 0;

GC = the number of G and C bases in the entire sense strand;

$Tm_{20^\circ C}$ = 1 if the Tm is greater than 20°C;

A_3 = 1 if A is the base at position 3 on the sense strand, otherwise its value is 0;

A_{11} = 1 if A is the base at position 11 on the sense strand, otherwise its value is 0;

A_{14} = 1 if A is the base at position 14 on the sense strand, otherwise its value is 0;

A_{19} = 1 if A is the base at position 19 on the sense strand, otherwise its value is 0;

U_5 = 1 if U is the base at position 5 on the sense strand, otherwise its value is 0;

U_{10} = 1 if U is the base at position 10 on the sense strand, otherwise its value is 0;

or,

Formula VIII: $(-14)*G_{13}-13*A_1-12*U_7-11*U_2-10*A_{11}-10*U_4-10*C_3-10*C_5-10*C_6-9*A_{10}-9*U_9-9*C_{18}-8*G_{10}-7*U_1-7*U_{16}-7*C_{17}-7*C_{19}+7*U_{17}+8*A_2+8*A_4+8*A_5+8*C_4+9*G_8+10*A_7+10*U_{18}+11*A_{19}+11*C_9+15*G_1+18*A_3+19*U_{10}-Tm-3*(GC_{total})-6*(GC_{15-19})-30*X$; and

Formula IX: $(14.1)*A_3+(14.9)*A_6+(17.6)*A_{13}+(24.7)*A_{19}+(14.2)*U_{10}+(10.5)*C_9+(23.9)*G_1+(16.3)*G_2+(-12.3)*A_{11}+(-19.3)*U_1+(-12.1)*U_2+(-11)*U_3+(-15.2)*U_{15}+(-11.3)*U_{16}+(-11.8)*C_3+(-17.4)*C_6+(-10.5)*C_7+(-13.7)*G_{13}+(-25.9)*G_{19}-Tm-3*(GC_{total})-6*(GC_{15-19})-30*X$

wherein

$A_1 = 1$ if A is the base at position 1 of the sense strand, otherwise its value is 0;

$A_2 = 1$ if A is the base at position 2 of the sense strand, otherwise its value is 0;

$A_3 = 1$ if A is the base at position 3 of the sense strand, otherwise its value is 0;

$A_4 = 1$ if A is the base at position 4 of the sense strand, otherwise its value is 0;

$A_5 = 1$ if A is the base at position 5 of the sense strand, otherwise its value is 0;

$A_6 = 1$ if A is the base at position 6 of the sense strand, otherwise its value is 0;

$A_7 = 1$ if A is the base at position 7 of the sense strand, otherwise its value is 0;

$A_{10} = 1$ if A is the base at position 10 of the sense strand, otherwise its value is 0;

$A_{11} = 1$ if A is the base at position 11 of the sense strand, otherwise its value is 0;

$A_{13} = 1$ if A is the base at position 13 of the sense strand, otherwise its value is 0;

$A_{19} = 1$ if A is the base at position 19 of the sense strand, otherwise if another base is present or the sense strand is only 18 base pairs in length, its value is 0;

$C_3 = 1$ if C is the base at position 3 of the sense strand, otherwise its value is 0;

$C_4 = 1$ if C is the base at position 4 of the sense strand, otherwise its value is 0;

$C_5 = 1$ if C is the base at position 5 of the sense strand, otherwise its value is 0;

$C_6 = 1$ if C is the base at position 6 of the sense strand, otherwise its value is 0;

C_7 = 1 if C is the base at position 7 of the sense strand, otherwise its value is 0;

C_9 = 1 if C is the base at position 9 of the sense strand, otherwise its value is 0;

C_{17} = 1 if C is the base at position 17 of the sense strand, otherwise its value is 0;

C_{18} = 1 if C is the base at position 18 of the sense strand, otherwise its value is 0;

C_{19} = 1 if C is the base at position 19 of the sense strand, otherwise if another base is present or the sense strand is only 18 base pairs in length, its value is 0;

G_1 = 1 if G is the base at position 1 on the sense strand, otherwise its value is 0;

G_2 = 1 if G is the base at position 2 of the sense strand, otherwise its value is 0;

G_8 = 1 if G is the base at position 8 on the sense strand, otherwise its value is 0;

G_{10} = 1 if G is the base at position 10 on the sense strand, otherwise its value is 0;

G_{13} = 1 if G is the base at position 13 on the sense strand, otherwise its value is 0;

G_{19} = 1 if G is the base at position 19 of the sense strand, otherwise if another base is present or the sense strand is only 18 base pairs in length, its value is 0;

U_1 = 1 if U is the base at position 1 on the sense strand, otherwise its value is 0;

U_2 = 1 if U is the base at position 2 on the sense strand, otherwise its value is 0;

U_3 = 1 if U is the base at position 3 on the sense strand, otherwise its value is 0;

U_4 = 1 if U is the base at position 4 on the sense strand, otherwise its value is 0;

U_7 = 1 if U is the base at position 7 on the sense strand, otherwise its value is 0;

U_9 = 1 if U is the base at position 9 on the sense strand, otherwise its value is 0;

U_{10} = 1 if U is the base at position 10 on the sense strand, otherwise its value is 0;

U_{15} = 1 if U is the base at position 15 on the sense strand, otherwise its value is 0;

U_{16} = 1 if U is the base at position 16 on the sense strand, otherwise its value is 0;

U_{17} = 1 if U is the base at position 17 on the sense strand, otherwise its value is 0;

U_{18} = 1 if U is the base at position 18 on the sense strand, otherwise its value is 0;

GC_{15-19} = the number of G and C bases within positions 15 – 19 of the sense strand or within positions 15 –18 if the sense strand is only 18 base pairs in length;

GC_{total} = the number of G and C bases in the sense strand;

Tm = 100 if the targeting site contains an inverted repeat longer then 4 base pairs, otherwise its value is 0; and

X = the number of times that the same nucleotide repeats four or more times in a row.

3. (original) A method of gene-silencing comprising selecting an siRNA according to claim 2 and introducing it into a cell.

4. (original) The method according to claim 3 wherein said introducing is by allowing passive uptake of the siRNA.

5. (original) The method according to claim 3, wherein said introducing is through the use of a vector.

6. (original) A method for developing an siRNA algorithm for selecting siRNA, said method comprising:
   (a) selecting a set of siRNA;
   (b) measuring the gene silencing ability of each siRNA from said set;
   (c) determining the relative functionality of each siRNA;
   (d) determining the amount of improved functionality by the presence or absence of at least one variable selected from the group consisting of the total GC content, melting temperature of the siRNA, GC content at positions 15 –19, the presence or absence of a particular nucleotide at a particular position and the number of times that the same nucleotide repeats within a given sequence; and
   (e) developing an algorithm using the information of step (d).

7. (original) A method of selecting an siRNA with improved functionality, said method comprising using the algorithm of claim 6.

8. (original) A method of selecting hyperfunctional siRNA, said method comprising using at least one functional siRNA, wherein at least one said functional siRNA has been selected according to the method of claim 7 and measuring the silencing ability of said at least one functional siRNA, wherein silencing ability is measured at a concentration of less than 1 nanomolar siRNA.

9.-18. (canceled)

19. (original) A kit, wherein said kit is comprised of at least two siRNA, wherein said at least two siRNA comprise a first optimized siRNA and a second optimized siRNA, wherein said first optimized siRNA and said second optimized siRNA are optimized according to one of the following formulas:

Formula I = $-(GC/3) + (AU_{15\text{-}19}) - (Tm_{20°C})*3 - (G_{13})*3 - (C_{19}) + (A_{19})*2 + (A_3) + (U_{10}) + (A_{14}) - (U_5) - (A_{11})$;

Formula II = $-(GC/3) - (AU_{15\text{-}19})*3 - (G_{13})*3 - (C_{19}) + (A_{19})*2 + (A_3)$;

Formula III = $-(GC/3) + (AU_{15\text{-}19}) - (Tm_{20°C})*3$;

Formula IV = $-(GC/2) + (AU_{15\text{-}19})/2 - (Tm_{20°C})*2 - (G_{13})*3 - (C_{19}) + (A_{19})*2 + (A_3) + (U_{10}) + (A_{14}) - (U_5) - (A_{11})$;

Formula V = $-(G_{13})*3 - (C_{19}) + (A_{19})*2 + (A_3) + (U_{10}) + (A_{14}) - (U_5) - (A_{11})$;

Formula VI = $-(G_{13})*3 - (C_{19}) + (A_{19})*2 + (A_3)$;

Formula VII = $-(GC/2) + (AU_{15-19})/2 - (Tm_{20°C})*1 - (G_{13})*3 - (C_{19}) + (A_{19})*3 + (A_3)*3 + (U_{10})/2 + (A_{14})/2 - (U_5)/2 - (A_{11})/2$;

wherein in Formulas I – VII:

AU_{15-19} = 0 – 5 depending on the number of A or U bases on the sense strand at positions 15 –19;

G_{13} = 1 if G is the base at position 13 on the sense strand, otherwise its value is 0;

C_{19} = 1 if C is the base at position 19 of the sense strand, otherwise its value is 0;

GC = the number of G and C bases in the entire sense strand;

$Tm_{20°C}$ = 1 if the Tm is greater than 20°C;

A_3 = 1 if A is the base at position 3 on the sense strand, otherwise its value is 0;

A_{11} = 1 if A is the base at position 11 on the sense strand, otherwise its value is 0;

A_{14} = 1 if A is the base at position 14 on the sense strand, otherwise its value is 0;

A_{19} = 1 if A is the base at position 19 on the sense strand, otherwise its value is 0;

U_5 = 1 if U is the base at position 5 on the sense strand, otherwise its value is 0;

U_{10} = 1 if U is the base at position 10 on the sense strand, otherwise its value is 0;

or,

Formula VIII: $(-14)*G_{13}-13*A_1-12*U_7-11*U_2-10*A_{11}-10*U_4-10*C_3-10*C_5-10*C_6-9*A_{10}-9*U_9-9*C_{18}-8*G_{10}-7*U_1-7*U_{16}-7*C_{17}-7*C_{19}+7*U_{17}+8*A_2+8*A_4+8*A_5+8*C_4+9*G_8+10*A_7+10*U_{18}+11*A_{19}+11*C_9+15*G_1+18*A_3+19*U_{10}-Tm-3*(GC_{total})-6*(GC_{15-19})-30*X$; and

Formula IX: $(14.1)*A_3+(14.9)*A_6+(17.6)*A_{13}+(24.7)*A_{19}+(14.2)*U_{10}+(10.5)*C_9+(23.9)*G_1+(16.3)*G_2+(-12.3)*A_{11}+(-19.3)*U_1+(-12.1)*U_2+(-11)*U_3+(-15.2)*U_{15}+(-11.3)*U_{16}+(-11.8)*C_3+(-17.4)*C_5+(-10.5)*C_7+(-13.7)*G_{13}+(-25.9)*G_{19}-Tm-3*(GC_{total})-6*(GC_{15-19})-30*X$

wherein

$A_1 = 1$ if A is the base at position 1 of the sense strand, otherwise its value is 0;

$A_2 = 1$ if A is the base at position 2 of the sense strand, otherwise its value is 0;

$A_3 = 1$ if A is the base at position 3 of the sense strand, otherwise its value is 0;

$A_4 = 1$ if A is the base at position 4 of the sense strand, otherwise its value is 0;

$A_5 = 1$ if A is the base at position 5 of the sense strand, otherwise its value is 0;

$A_6 = 1$ if A is the base at position 6 of the sense strand, otherwise its value is 0;

$A_7 = 1$ if A is the base at position 7 of the sense strand, otherwise its value is 0;

$A_{10} = 1$ if A is the base at position 10 of the sense strand, otherwise its value is 0;

$A_{11} = 1$ if A is the base at position 11 of the sense strand, otherwise its value is 0;

$A_{13} = 1$ if A is the base at position 13 of the sense strand, otherwise its value is 0;

$A_{19} = 1$ if A is the base at position 19 of the sense strand, otherwise if another base is present or the sense strand is only 18 base pairs in length, its value is 0;

$C_3 = 1$ if C is the base at position 3 of the sense strand, otherwise its value is 0;

$C_4 = 1$ if C is the base at position 4 of the sense strand, otherwise its value is 0;

$C_5 = 1$ if C is the base at position 5 of the sense strand, otherwise its value is 0;

$C_6 = 1$ if C is the base at position 6 of the sense strand, otherwise its value is 0;

$C_7 = 1$ if C is the base at position 7 of the sense strand, otherwise its value is 0;

C_9 = 1 if C is the base at position 9 of the sense strand, otherwise its value is 0;

C_{17} = 1 if C is the base at position 17 of the sense strand, otherwise its value is 0;

C_{18} = 1 if C is the base at position 18 of the sense strand, otherwise its value is 0;

C_{19} = 1 if C is the base at position 19 of the sense strand, otherwise if another base is present or the sense strand is only 18 base pairs in length, its value is 0;

G_1 = 1 if G is the base at position 1 on the sense strand, otherwise its value is 0;

G_2 = 1 if G is the base at position 2 of the sense strand, otherwise its value is 0;

G_8 = 1 if G is the base at position 8 on the sense strand, otherwise its value is 0;

G_{10} = 1 if G is the base at position 10 on the sense strand, otherwise its value is 0;

G_{13} = 1 if G is the base at position 13 on the sense strand, otherwise its value is 0;

G_{19} = 1 if G is the base at position 19 of the sense strand, otherwise if another base is present or the sense strand is only 18 base pairs in length, its value is 0;

U_1 = 1 if U is the base at position 1 on the sense strand, otherwise its value is 0;

U_2 = 1 if U is the base at position 2 on the sense strand, otherwise its value is 0;

U_3 = 1 if U is the base at position 3 on the sense strand, otherwise its value is 0;

U_4 = 1 if U is the base at position 4 on the sense strand, otherwise its value is 0;

U_7 = 1 if U is the base at position 7 on the sense strand, otherwise its value is 0;

U_9 = 1 if U is the base at position 9 on the sense strand, otherwise its value is 0;

U_{10} = 1 if U is the base at position 10 on the sense strand, otherwise its value is 0;

U_{15} = 1 if U is the base at position 15 on the sense strand, otherwise its value is 0;

U_{16} = 1 if U is the base at position 16 on the sense strand, otherwise its value is 0;

U_{17} = 1 if U is the base at position 17 on the sense strand, otherwise its value is 0;

U_{18} = 1 if U is the base at position 18 on the sense strand, otherwise its value is 0;

GC_{15-19} = the number of G and C bases within positions 15 – 19 of the sense strand or within positions 15 –18 if the sense strand is only 18 base pairs in length;

GC_{total} = the number of G and C bases in the sense strand;

Tm = 100 if the targeting site contains an inverted repeat longer then 4 base pairs, otherwise its value is 0; and

X = the number of times that the same nucleotide repeats four or more times in a row.